

HUMAN TISSUE SAMPLES FOR RESEARCH. A FOCUS GROUP STUDY IN ADULTS AND TEENAGERS IN FLANDERS

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Summary: Human tissue samples for research. A focus group study in adults and teenagers in Flanders: Attitudes towards research on human stored tissue samples may be dependent on the cultural context. To-day, no data exist on the attitudes and values of the Flemish population towards such research. To query these attitudes, we conducted ten focus groups, composed of adults and of minors on the verge of legal competence. Amongst the focus group participants, we found a trust in the advancement of science, and a willingness to contribute tissue to research. The importance attributed to informed consent depended on the type of tissue donated and the effort needed to contribute. Participants did not see high risk associated with research on stored tissue, but thought there was a need for confidentiality protections. The coding of samples was deemed an appropriate protection. With regard to the return of research results, people expected to receive information that could be relevant to them, but the meaning of what is relevant was different between individuals.

Key-words: Biological sample collections – Focus group – Informed consent – Confidentiality – Biobank – Ethics.

INTRODUCTION

The storage and use of human tissue samples for biomedical research is much discussed. A substantial corpus of empirical literature exists, querying people's attitudes towards donating tissue for medical research. In the following paragraphs we have included only references from 2006 upwards, except for the focus group studies. This literature consists of qualitative and quantitative studies, such as surveys (8, 9, 10, 14, 17, 18, 19, 21), interviews (4, 5), focus group studies (1, 2, 12, 15, 16, 24, 25) and a review of the empirical literature (26). Themes investigated and discussed in the literature are attitudes towards research (5, 10, 12, 25), willingness to donate (9, 10, 19), commercialization (4, 5, 12, 17), consent (4, 8, 19, 21, 22, 26), risks (5, 8, 18) and return of results (6, 14, 15, 18, 20, 21).

With regard to general attitudes towards research and science and willingness to participate, studies found that these attitudes were mostly quite positive (5, 10). Only cloning was sometimes mentioned as unacceptable (5). One UK study found that medical research had a positive image, but that trust was starting to erode (25). With regard to genetic research, this study found that the more it was understood, the better

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it was appreciated. In a study by Levitt, people saw genetic data as special (12). Also the willingness to donate tissue was quite high in most studies (10, 19). It was linked with the level of trust they had in biomedical research (9).

In an Austrian study, people rejected the idea of being compensated for donating tissue, as they saw their donation as an act of solidarity (5). A UK study found that some people were worried that they would donate freely, but that their donation was used to make money (12). Information and consent was seen as more important if the research was done for financial gain (17).

It is widely accepted in guidelines and ethical and legal literature (7) that the donor or patient whose biological material is used, should give informed consent, and that adequate privacy protection measures should be put in place. Although it is seen as good ethical practice to ask for consent (4), a US study found that people found consent less important when anonymous samples were used (8). A meta-analysis by Wendler showed that most participants would prefer broad consent (26). A survey of American and Spanish geneticists showed that they obtained narrow consent but would prefer to be allowed to obtain broad consent (21).

In a US-based study by Ormond, the majority of participants did not see any risks associated with biobank research. A minority quoted confidentiality breaches and the risk that insurers and employers would access this information (18). Also in the US, Hull found that the preferences of patients with regard to storage and use of their tissue were independent of whether these tissues were kept identifiable or not (8). An Austrian study found that there was no real concern about privacy protection (5).

A topic that is still hotly debated in ethical literature is whether researchers should return accidental findings to participants (6). A US-based study showed that most would want to have a choice whether to receive results or not (15). Another US-based study found that a majority of participants either hoped for or desired being recontacted with accidental findings (18). A Japanese study found a high level of positive preference for future disclosure of individual genetic results (14). In a survey of Spanish and American geneticists, the majority of geneticists wanted to inform participants of reliable results (21).

Today, no data exist on the attitudes of the Flemish population towards research on stored tissue samples. As such attitudes may be dependent on cultural context we found it useful to query these attitudes and opinions (11). Specifically, we discussed attitudes and ethical values with regard to research on stored tissue samples, commercialization, willingness to donate samples, the importance of informed consent

and ethics committees, the risks they saw associated with stored tissue samples and the return of research results. Because we wanted to explore these questions into some depth, and find out whether there were any issues that did not come up in the existing literature, we chose focus groups as our *modus operandi* (13). As we did not find any empirical studies based on the opinions of young people on the verge of majority, which is 18 in Belgium, we also conducted focus groups in this age group.

MATERIALS AND METHODS

We conducted focus groups to investigate the concerns of a Belgian population with regard to research on stored tissue samples. Our study group conducted 10 focus groups with a total of 76 participants from February 2009 through March 2009. We provided food and beverages, so that even when the focus groups were conducted in environments such as schools, people would feel relaxed. The focus group with parents from children with a medical condition was performed online, through a chat room, as we thought that the travel distance would be an impediment for participation in this group (23). We have provided an overview of the different focus groups in table I. We developed standard qualitative focus group procedures (13). The topics the moderator (Kristien Hens) introduced during the discussion were the willingness to donate samples for biomedical research, the need for consent and information, the possible dangers they thought were associated with such research, the role of ethics committees, the need to return incidental research findings. We conducted a pilot focus group with specialists in medical law, medical ethics and social sciences, and reviewed the discussion guide based on the outcome of the pilot. We used three different scenarios: the use of surgical waste, the use of blood that was gathered in the context of a medical examination, and a longitudinal cohort study (see table II). The scenarios and topics were not introduced at fixed moments in the discussion, but as the moderator deemed appropriate based on the discussion flow.

The discussion groups were conducted with Kristien Hens (KH) as a moderator. Kris Dierickx (KD) was assistant-moderator in most of the groups. At the beginning of each discussion, the participants were told that the talk was audio taped and that we would process our findings in a publishable report. They were assured that this report would contain only anonymous data. No one objected. Audiotapes of the sessions were transcribed but not corrected for grammar, in order to capture the oral nature of the discussion.

Table 1: Overview of focus groups

Focus Group	Number of males/females	Age range	Type of discussion	Duration of discussion	Recruitment method	Additional information
FG1	5 Female, 3 Male	15-16	Live	60 minutes	One teenager was asked to gather mixed group of different schools	Mixed group: catholic and public schools, secondary and technical education
FG2	8 Female	24-48	Live	1h45 minute	Internet forum (about motherhood) and women's organization	Group composed of mothers
FG3	6 Female, 1 Male	16-17	Live	50 minutes	Recruitment through teacher from public school	Pupils from one class in a public school
FG4	3 Female, 1 Male	26-73	Live	1h30 minutes	Recruitment through the Flemish platform of patient's organizations	Group composed of members from different patients' organizations
FG5	4 Female, 4 Male	16-19	Live	60 minutes	Recruitment through board of Steiner school	Pupils from different classes of a Steiner school
FG6	5 Female, 4 Male	31-52	Live	1h30 minutes	Recruitment through internet fora and local community organizations	Mixed group
FG7	9 Female, 1 Male	61-77	Live	1h15 minutes	Recruitment through organization of senior citizens	Senior citizens
FG8	3 Female, 1 Male	28-49	Online	60 minutes	Recruitment through parents' internet fora and the national cystic fibrosis organization	Parents of children with a medical condition
FG9	4 Female, 5 Male	16-17	Live	45 minutes	Recruitment through board of Catholic school	Pupils from different classes from General Secondary Education in a Catholic school

Table II: Overview of scenarios and associated questions

Scenario	Description
Use of surgical waste	Imagine a cancer patient undergoing an operation. His or her tumor is removed. Afterwards, this tumor can be used for research on cancer. Would you consider this a good thing? If you were in this situation, would you want to be informed about such research? Would you want to give permission? Do you see any problems with the use of tumors for research?
Use of blood	Imagine a routine medical checkup at the doctor's office. This checkup requires some blood to be drawn for analysis. The doctor asks whether he or she can draw some extra blood that is to be used for research. Do you think this scenario is different from the previous one? Would you mind that your blood is used? Would you want to know about such research? Would you put any restrictions on the type of research that can be done on this blood?
Longitudinal study	Imagine a study that follows participants over a period over several years. Research participants are asked to yearly give some blood for research and to undergo some medical examinations and some tests, such as an IQ test. This research is done for the advance of science not to know about the health of participants. Do you think such research is useful? Would you participate to such research? Under which conditions?

We used NVIVO8 to do a detailed coding of the transcripts and to compare between focus groups and participants. NVIVO is a qualitative data analysis software package especially suited for analysis of qualitative data such as focus groups transcripts (3). We created cases for each focus group participant, with attributes containing demographic values to allow for comparison between groups and participants. During a first-pass analysis, we performed descriptive coding to assign each piece of text to a case. During a second pass analysis, we did a detailed coding according to the various topics in the text. This part of the coding was done by KH and KD separately and then compared to match themes. Most groups were quite uniform in their opinions, but we have pointed out the most striking differences between groups in the results sections. In the rest of this paper, we discuss the findings related to attitudes, commercialization, willingness to participate, consent, ethics committee oversight, risks and return of results.

RESULTS

ATTITUDES AND COMMERCIALIZATION

All focus group participants thought that research on stored tissue samples was useful: they quoted the discovery of new medicine, as well as fundamental research on the functioning of DNA and genes and the development of cancer cells. The uses of human biological materials that were seen as unacceptable were, apart from cloning, outside of the biomedical sphere and included biological warfare and consumer products such as cosmetics. Although we did not specifically introduce the topic of commercialization, this was a topic that came up spontaneously, except for two of the five teenager focus groups. With regard to the use of their own tissue by pharmaceutical companies, reactions ranged from indifference to reluctance. People holding the latter attitude would prefer to donate to universities. However, the same people often came to the conclusion that commercial research might also be necessary for the advance of science. There was some fear about excesses if pharmaceutical companies performed biomedical research: patenting should not stall research or make innovations inaccessible to patients. Also, people thought it acceptable that companies would make money out of a scientific finding based on samples, but not out of the direct selling of a sample.

WILLINGNESS TO PARTICIPATE AND CONSENT

All participants would agree to the use of leftover tumors for research, but were divided on whether this could be used with or without consent. One line of thought was that it was not needed to ask permission, as it would be thrown away otherwise. Another view was that researchers should ask it anyway, out of politeness, as donation might be against someone's religious beliefs. But others expressed the fear that if such permission was asked, some people would refuse and hence valuable material would get lost.

In this scenario, the line between information and consent was difficult to draw: On the one hand, participants believed it was good that patients knew that their tumor would be used for further research, to aid other people. On the other hand, participants also feared that such patients would be burdened by too much information.

The second scenario we dealt with was the collection of an 'extra tube of blood for research', in the context of a routine medical checkup. This was considered different from the tumor, although participants found it hard to specify why. They agreed almost unanimously that if

an extra tube of blood was taken for research, consent should be sought. But many participants were also willing to contribute to this type of research. In this scenario many participants would like to receive further information about the type of research. The more trustful participants, however, stated that they would equally well donate blood in this case, regardless of the type of research that was performed.

When participants reflected on the third scenario, of a longitudinal research on biobank samples, all participants in all focus groups agreed that this would have to be on a voluntary basis. But also here, there was willingness to participate. Those unwilling were not adverse to the research as such, but were afraid it would cost them too much time, or thought punctures were too troublesome to have done on a regular basis.

ETHICS COMMITTEE OVERSIGHT

There was a consensus that ethics committee supervision of research on stored tissue samples was a good thing. Participants would be willing to rely on the opinions of ethics committees to decide on the usefulness and acceptability of research. The fact that they would know that an ethics committee was involved was felt to be a reassurance. The task of such ethics committee would not only be to decide on the acceptability of research, but, some thought, also to prioritize and to decide which research is more important and should be performed first. In one adult focus group, people would even accept surrogate decision making by ethics committees, and hence were willing to delegate their responsibility to decide which research was acceptable or not. In the other groups, this was less pronounced. As for the members of ethics committees, there was consensus that these should consist of medical experts, but some also mentioned lawyers, ethicists, lay people and representatives of different religions.

RISKS ASSOCIATED WITH RESEARCH ON STORED TISSUE SAMPLES

Apart from the fact that some participants did not like venepunctures, people did not associate too much risk with research on stored tissue samples. If risks were quoted, they were related to privacy issues. People thought there should be some assurance that only the researchers could access the data. In a focus group with teenagers, the suggestion was made that some people would be 'ashamed' if they had a disease such as AIDS and this would be widely known. Employers and insurance companies were sometimes mentioned as instances that

should not have access to medical information and biological samples. Also, there was fear that representatives of pharmaceutical companies and even supermarkets would use these data for targeted marketing. But participants did not have problems with sharing medical information next to biological samples with biomedical researchers.

We discussed the link between traceability of biological samples and medical data and confidentiality. For more distrustful participants, anonymization was a requirement for participation, as this would be an absolute guarantee that no information could be leaked to third parties such as insurance companies. But it was acknowledged that anonymization did have some drawbacks: researchers would not be able to contact participants for further background information and if something relevant to the participant was found, there was no way this could be returned.

In the majority of the focus groups, the solution of coding was spontaneously suggested as an acceptable middle ground between total anonymization and complete identifiability.

RETURN OF RESULTS

One topic that was discussed in some depth in most of the focus groups was whether researchers would have the duty to return incidental findings to participants. On the one hand, people accepted that there is a clear distinction between research and diagnosis, and that the focus of the former is not to provide diagnostic information to individual participants. On the other hand, returning results was considered the more humane option. Also, returning personal results was sometimes seen as a kind of compensation for the effort of participating research. There was much disagreement, however, about which types of results should be returned. There was some consensus that preventable and treatable conditions should be told. In this context, contagious diseases such as AIDS were quoted. However, when an example such as Alzheimer came up, there was disagreement whether people wanted to know this or not. Some groups concluded that it might be best to ask donors and patients whether they would want results or not, and even which type of results they wanted.

Participants also discussed the possibility of receiving general (non-personal) research results. Reactions ranged from indifference to whether they received such information or not to appreciation. Appreciation was linked to being more motivated and to being able to feel proud if people knew to which research they had contributed. Especially in the focus group of representatives of patient organizations it was stated that in any case these results should be understandable for lay people.

DISCUSSION

As a whole, we found a strong interest in science and a strong feeling of commitment. People used terms as pride and curiosity when they referred to their potential donation to scientific research. Belgium is a welfare state with a well established social security system and has been unaffected by scandals in medical practice or medical research, which can explain the trust in science we found. This is also consistent with studies in countries such as Sweden and Austria (5, 10), and slightly different from studies in the UK, which has recently been affected by the Alder Hey scandal (25). The view of science as something which is linearly progressing is similar to what Felt describes, with a reference to Godin, as a linear flow of progressing innovation, to benefit humankind and create better futures (5). As she describes, this is linked with a high willingness to donate tissue. The fact that most of our participants were not completely negative to the use of samples by pharmaceutical companies might also be linked to this. On the one hand, non-profit research in universities and hospitals is seen as being at the core of the medical practice, with first right of access to samples. On the other hand, pharmaceutical companies, which are companies that function within the same medical practice, are considered as valuable for progress as well. Mary Dixon-Woods speaks in this respect of a mixed economy (4). People agreed that uses that fall outside of medical practice, such as cosmetics and direct marketing, were not acceptable.

Broadly, we could identify ranges from extremely trustful people to people that were less trustful and had some reservations. People from the first category were typically happy to contribute to any kind of research, would not mind tissue being used even without consent, would not mind identifiable samples to be used, saw no risk associated to research and were happy to rely on ethics committees for ethical decision making. Informed consent and information were seen as a 'nice to have'. People from the latter category would prefer anonymous samples, as they had greater fear that third parties would gain access to and misuse information derived from biological samples. They attributed greater importance to informed consent in comparison to surrogate decision making by ethics committees. But still, they had a fairly high confidence in science and scientists as such. Most participants fell in between these two categories.

With regard to the tasks of informed consent, our findings were consistent with other empirical studies that query the task of informed consent (5, 12). Informed consent was not primarily aimed at the need to make an informed choice based on risk, although for the participants

that belonged to the category ‘distrustful’ this also played a role. The fact that scientists would ask permission or at least give information was considered overall as positive, and a sign of ‘respect’ but more so in scenarios two and three. This was linked to the higher level of effort that people thought was required in these cases. With regard to the need to consent for residual materials, opinions were divided. Overall information and consent were seen as a nice to have: people would not mind leftover materials to be used, but would also be curious about research performed on these materials. However, for some of our more distrustful participants, consent was also an absolute requirement in the case of residual materials.

Participants did not see much danger in contributing tissue and medical data for research. Risks quoted were linked with confidentiality issues, the use of that data by third parties such as employers and insurers, and sometimes the fear of being associated with a certain disease. This is analogous with existing empirical data that quote breach of privacy, confidentiality & reputation (8, 15, 18). The solution of coding samples and data, as was spontaneously suggested, was thought sufficient to protect against these risks.

With regard to returning of results, the fact that people would receive general research results, or could enroll to receive such information, is perceived as positive, which is consistent with a UK study that found that most people like to receive such results (8). With regard to the return of individual results, the discussion is somewhat more difficult. Although people are aware that medical research is for the benefit of future patients, there seems to be an expectation that important findings are communicated to the afflicted donor. This is consistent with empirical studies in other countries (14, 18, 21). However, it was unclear exactly which findings should be returned: this ranged from anything that might be significant to only contagious diseases such as HIV.

Participants in the teenage groups showed a great confidence towards scientists and a great trust that science is useful. They also showed much curiosity in research findings. The teenagers were overall not much concerned with privacy protections, and did not mention the risk of unauthorized access by insurers or employers. The greatest privacy concern that was voiced in these groups was that of stigmatization, of people being ashamed of having a certain disease.

We acknowledge that our study has several limitations. We had a very small number of participants in focus groups FG4 (members of patient organizations) and FG8 (parents of children with a medical condition), and a small number of males (7 males – 28 females) in the focus groups with adults which made our study sample somewhat unbalanced. Also,

given the qualitative nature of our study our findings can probably only hint at what lives in the minds of the Belgian population. Ideally, such study is followed by a larger population-wide quantitative study, which would allow more detailed analysis of differences between categories of people. However, given the fact that this is the first study of opinions about the subject in Flanders, and of the opinions of teenagers on this matter, and that we got fairly homogenous responses, we think that it is a good 'first step'. The fact that it is a focus group study, on a voluntary basis, also implies that the participants might have been biased, either in the positive or the negative sense, and is probably not representative of the Flemish population.

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